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EXAMINER

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. 17

Application Number: 09/540236
Filing Date: 04/03/2000
Appellant(s): Fisher et al.

Lawrence M. Lavin, Jr.
For Appellant

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EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 05/02/2003.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

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The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejections of claims 1,2,4-7 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is not exactly correct. The claim presented as claim 3 is, in fact, claim 4. The real claim 3 is drawn to a protein and is withdrawn from consideration.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

Claim Rejections - 35 U.S.C. § 101/ 112-1

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Claims 1,2,4-7 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well established utility. The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The invention as claimed is drawn to nucleic acids comprising SEQ ID No.1 (claims 1,2), and correspondent cells comprising said SEQ ID No.1. Nucleic acid of SEQ ID No.1 is isolated from cDNA library of *Cyanidium caldarium*, which is an acidophilic and thermophilic algae existing in thermal areas. Nucleic acid of SEQ ID No. 1 itself is not supported by a specific asserted utility because the uses disclosed in general for all nucleic acids (SEQ ID Nos. 1 to 5674) are not specific and are generally applicable to any nucleic acid. No open reading frame, start/stop codons, or encoded protein is identified in the specification for SEQ ID NO. 1. No information about a protein encoded by the particular SEQ ID NO. 1 is provided. The specification states that the nucleic acid compounds may be useful as probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to make the corresponding antibodies, plants, gene mapping,

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isolation of homologous sequences, detection of gene expression, and for numerous other generic genetic engineering usages, such as detection of polymorphisms. These are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acid of SEQ ID No. 1 being claimed. Further, the claimed nucleic acid compounds are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In the instant case none of *Cyanidium caldarium* proteins (and much less so much fragments of such proteins) have a specific or substantial utilities. The research contemplated by applicants to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth

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above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid compounds such that another non-asserted utility would be well established for the compounds.

Claims 1,2,4-7 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

(11) Response to Argument

Claim Rejections - 35 U.S.C. § 101/ 112-1

Appellants assert that the claimed invention meets the utility and enablement requirements because they have disclosed "nucleic acid molecules which, in their current form provide at least one specific benefit to the public, for example use to identify the presence or absence of a polymorphism." The examiner does not agree that the nucleic acid molecules provide any specific benefit to the public in their current form but rather require further experimentation to determine whether such a benefit can be found.

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The Examiner agrees that the “The threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit,” with the proviso that the benefit be “identifiable” in the original disclosure either as a specific assertion or being readily apparent from the disclosure (i.e. well established). The Examiner also agrees “the invention must have specific, i.e. not vague or unknown benefit” and “must provide a real world, i.e. practical or substantial, benefit.” Whether the instant application has met this burden is the subject of this section of the appeal.

Appellant argues (p.5, last paragraph) that the claimed nucleic acid molecules can be used to detect the presence and/or identity of polymorphisms, as hybridization probes for expression profiling, for genetic mapping or monitoring gene expression, as antisense inhibitors, and as a molecular marker. The Examiner maintains that further research is required for such uses.

MPEP 2107 states that:

On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a “real world” context of use and, therefore, do not define “substantial utilities”:

- (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
- (B) A method of treating an unspecified disease or condition;
- (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
- (D) A method of making a material that itself has no specific, substantial, and credible utility; and
- (E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

All of these situations closely match appellant's disclosed uses. They do not define substantial utilities. Further, MPEP 2107 states

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An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

The instant specification sets forth no such correlation for any such conditions.

With respect to use of nucleic acids as probes in microarrays, specification does not associate any of the claimed sequences with any trait of interest. Contrary to appellant's assertions, further experimentation is required to identify a "real world use." A negative result to such a screen tells what the nucleic acid is not and cannot be used for. A positive result to such a screen requires further experimentation to determine what, if anything, such a change means. It is not an immediate benefit except in the sense to indicate that further research might yield a "real world use."

With respect to use of nucleic acids for detecting polymorphisms, the brief on page 6 discusses gas chromatograph. MPEP 2107 in discussing research tools sets forth the following:

Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm. Labels such as research tool, "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention.

Again, further experimentation is required to use determine and confirm any of the uses set forth by appellant for the claimed nucleotide sequences.

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The gas chromatograph example set forth by appellant, particularly as discussed in Footnote 5 on page 7, is not analogous to the present disclosure. A gas chromatograph is a piece of equipment designed and built for a particular use. Such equipment is fully tested, evaluated, and calibrated to ensure accurate results. Those skilled in the art use gas chromatographs to analyze both known and unknown compounds. When the compound is unknown, the results obtained are compared to results for known compounds, e.g. standards. Appellants did not design the claimed nucleotide sequences for any particular purpose. They merely isolated them. They have not tested, evaluated, or calibrated the claimed nucleotide sequences for any particular use. Sampling for the presence or absence of chlorine in a crude oil sample is not analogous to the present situation. The presence or absence of chlorine in a crude oil sample has a known meaning based upon prior research. Absent establishment of this association between presence of chlorine and destruction of catalyst, the presence or absence of chlorine in a sample would not provide any useful information to the refinery manager. Likewise, the presence or absence of any of the claimed nucleotide sequences in a sample (or polymorphisms thereof) has no meaning absent some association. Further experimentation is required to determine what that meaning or association might be.

In addition, this gas chromatograph analogy fails address Appellants' own definition of the term polymorphism. The specification (page 94, line 5 +) defines "polymorphism" as "a variation or difference in the sequence of the gene or its flanking

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regions that arises in some members of a species.” It follows from this definition that if there is no “variation or difference in the sequence of the gene or its flanking regions” among “members of a species,” then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome. A “polymorphism” is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the *presence* of a polymorphism by analyzing multiple members of the species, i.e. analyzing a population. While one can detect the absence (or presence) of a specific allele of the polymorphism in a specific individual member of the species, one cannot detect the *absence* of a polymorphism *per se* based on one individual alone. The absence of a particular allele necessarily means that a different allele is present. The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect. With respect to the gas chromatograph analogy, one can only detect the absence of a compound, such as chlorine, in a sample, *if* it was already known that chlorine could, in fact, be detected by the gas chromatograph were it present in the sample.

The specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or

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a specific polymorphism that could be detected ¹. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest. The court in *Kirk* (at page 53) held:

We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.

The specification (page 94, line 5 +) defines “polymorphism” as “a variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species” (emphasis added). The following pages of the specification discuss various types of sequence polymorphisms and how they are detected. It is noted that on page 97, lines 15-17, the specification states, “By correlating the presence or absence of it [a polymorphism] in a plant with the presence or absence of a phenotype...”. Thus, the specification acknowledges that further analysis is required to determine a use for a polymorphism even assuming one is found. A change of phenotype and correlation with phenotype must be found; linkage analysis must be performed.

¹ It is noted that even though polymorphisms are discussed on pages 94-95 of specification, the first reference to polymorphisms in the Brief (p. 6, lines 3-4) refers to page 92, lines 15-18, of specification as describing use of nucleic acids to “identify the presence or absence of polymorphism”. However, the indicated part of specification is devoid of discussing the issue of polymorphism.

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Even to determine whether a polymorphism exists at a specific chromosomal location requires hybridization to at least two individual chromosomes, and generally involves analyzing genomic DNA from multiple members of a species; the specification discloses no such analysis. The specification fails to disclose: 1) whether the claimed nucleic acid molecule can in fact detect a polymorphism, or even whether such a polymorphism exists; and 2) at least one specific example of at least one of the types of polymorphisms described in the specification. The specification does not disclose any utility in this context for a nucleic acid molecule or EST that can NOT detect a polymorphism. Therefore, using the claimed invention to first determine whether or not the claimed nucleic acid molecule can, in fact, detect a polymorphism *is* to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is "use testing" and not substantial. Since the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms.

Appellants argue that the claimed nucleic acid molecules have utility as "probes for other molecules or as a source of primers." Appellant argues that the claimed nucleic acid molecules are useful to detect or measure nucleic acid

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molecules that possess a certain level of structural relatedness to the claimed nucleic acid molecules, the level of relatedness being defined by hybridization to the claimed nucleic acid molecules. However, the specification discloses *no* nucleic acid molecule that hybridizes with the claimed nucleic acid molecules that does *not* consist or comprise SEQ ID NO:1 or its complement. In order for hybridization between two nucleic acid molecules to occur, they must share at least some nucleotide sequence that is fully complementary. The length of fully complementary sequence required to detect hybridization depends primarily on the stringency of the specific hybridization conditions employed, the lower the stringency the shorter the length of fully complementary sequence required. The specification also fails to disclose any hybridization conditions required for detecting nucleic acid molecules that do *not* contain the nucleotide sequence of SEQ ID NO: 1 or its complements (other than subsequences of SEQ ID NO:1), in addition to failing to disclose any source for such nucleic acid molecules.

All arguments pertaining to the utility of the claimed invention with respect to studying the corresponding genomic DNA and mRNA found in soybean, would also apply to any homologous nucleic acid molecules found in other algae species. In so much as the specification fails to describe a specific and substantial utility for the corresponding nucleic acids in lily, so does it fail to describe a specific and substantial utility for the corresponding nucleic acids in other algae species.

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Appellants cite *Carl Zeiss Stiftung v. Renishaw PLC* (p.11) in support of their position that utility has been established. However, this decision is with respect to a mechanical device and not a laboratory reagent or research tool. Furthermore, applicant mischaracterizes the findings in this decision. This decision concerned claim interpretation and the CAFC found that the district court had erred in their interpretation of what the claim embraced and thus what was required to establish utility. The claimed device was found to fulfill the stated objective of mounting a stylus by the CAFC. These facts do not correspond to the instant specification

With respect to to use of the claimed nucleic acids to obtain other nucleic acid molecules, the specification does not indicate that any such nucleic acid molecules had been obtained, nor does it describe any characteristics possessed by such nucleic acid molecules. As to whether such molecules could, in fact, be obtained, the Office can neither prove nor disprove the assertion because the Office does not have laboratory facilities. At the time the application had been filed, future experimentation on the part of one skilled in the art would have been required to determine which, if any, other algae species contained nucleic acid molecules that could have been obtained using the claimed invention, and under what experimental conditions.

With respect to using the claimed nucleic acid molecules to initiate a chromosome walk, such as to isolate a promoter of the corresponding gene, the

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specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within "chromosome walking" distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined.

In this context, the claimed invention does not compare to a golf club, because one knows what a golf ball is and how to use the golf club to hit it, whereas the specification does not disclose or describe with particularity any known useful nucleic acid molecule that can be obtained, such as the corresponding promoter - it simply invites the skilled artisan to provide such information by further experimentation.

Even assuming *arguendo* that the corresponding promoter exists is no more guidance for its isolation, and eventual use, than knowing that a haystack contains a needle - at least one is presumed to know what the needle looks like. Also, the specification does not disclose the distance or direction one has to walk on a chromosome from the corresponding location to reach the corresponding promoter. Thus, starting the walk at the corresponding chromosomal location is no more help in identifying the promoter than is picking a specific location in a haystack to start looking for a needle when one does not know where the needle is relative to the starting location. Initiation of a chromosome walk at the corresponding chromosomal location is considered

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non-specific because any EST would serve the purpose for isolating an uncharacterized promoter, since any chromosomal location is expected to be linked to a promoter. The specification fails to disclose sufficient characteristics of the corresponding promoter, such as its sequence or precise location relative to the genomic location corresponding to the claimed nucleic acid molecule, to inform one of what the corresponding promoter is or when it has been isolated. For example, a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cell, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells. Substantial utility means that "one skilled in the art can use a claimed discovery in a manner which provides some *immediate* benefit to the public," *Nelson v. Bowler*, 206 USPQ2d 881, 883 (CCPA 1980) (emphasis added). Since the specification does not describe the corresponding promoter, or any other specific nucleic acid molecule, sufficient to inform one skilled in the art that it has been isolated, there can be no "*immediate* benefit to the public" in using the claimed nucleic acid molecule in this capacity; "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion," *Brenner* at page 696.

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With respect to the “real world” value of ESTs in general (brief, pages 9,10), it is asserted that there is “no question that the public has recognized the benefits provided by the claimed subject matter, “ it is unclear as to what evidence Appellants are alluding. The evidence supplied by Appellants shows that a multimillion dollar industry has arisen surrounding buying and selling EST databases and clones, not that anyone in this industry has bought or sold the claimed subject matter. It is noted that simply because a product, such as an EST sequence database or clone library, is bought and sold does not mean it has patentable utility.

With respect to credibility, appellant is reminded that in order to meet the requirements of 35 USC 101, the specification must disclose at least one utility that is specific and substantial, as well as credible (absent a showing of well established utility, which would presume that the utility was credible). The claims have been rejected because 1) the specification fails to disclose at least one utility that is both specific and substantial, and 2) no convincing evidence has been presented to show that an EST, for which only its nucleotide sequence and source have been disclosed, has a well established utility.

The brief does not appear to directly argue for a well established utility for the claimed invention; however, the arguments concerning the commercial value of ESTs in general (brief, page 10) may implicitly be directed to a well

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established utility for any EST in general, and the claimed nucleic acid molecules in particular. However, such evidence is not relevant to 35 USC 101.

C. *Claim Rejections - 35 U.S.C. § 112-1 (enablement)*

The Examiner maintains that the uses asserted for the claimed invention are methods where the claimed invention is, itself, an object of scientific study, e.g. to determine whether the corresponding genomic DNA of lilies contains a polymorphism that can be detected with the claimed invention. The specification cannot enable or tell how to use the invention within 35 U.S.C. 112, first paragraph, if there is no patentable utility within 35 U.S.C. 101. The Examiner maintains that there is no patentable utility for the claimed invention for the reasons set forth above and thus the claims are not enabled.

For the above reasons, it is believed that the rejections should be sustained.

Respectively submitted

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